REMARKS/ARGUMENTS

The Pending Claims

Claims 1-3, 6-19, 21, and 42-58 are pending. Claims 2, 3, 11, 12, and 42-58 are withdrawn as being drawn to a non-elected invention in response to a restriction requirement. Thus, claims 1, 6, 10, 13-19, and 21 currently are under examination.

The Amendments to the Claims

Claim 1 has been amended to recite a gene transfer vector comprising a nucleic acid sequence encoding an exotoxin of *Bacillus anthracis*, to clarify that the nucleic acid sequence encoding the exotoxin comprises SEQ ID NO: 1, and to clarify that the gene transfer vector also comprises a nucleic acid sequence encoding a heterologous sorting signal. This amendment is supported by the specification at, for example, paragraph [0008]. Claim 21 has been amended to delete the term "pharmaceutical." Accordingly, no new matter has been added by way of these amendments.

The Office Action

The Office Action rejects claims 6 and 7 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office Action rejects claims 1, 6-10, 13-19, and 21 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description and enablement. Reconsideration of these rejections is respectfully requested.

Discussion of Rejection Under 35 U.S.C. § 112, Second Paragraph

The Office Action rejects claims 6 and 7 under Section 112, second paragraph, as allegedly indefinite. Specifically, the term "exotoxin" in claim 6 allegedly lacks proper antecedent basis. Claim 1 has been amended to recite a nucleic acid sequence encoding an exotoxin of *Bacillus anthracis*. Thus, the rejection of claims 6 and 7 is rendered moot by this amendment, and the rejection under Section 112, second paragraph, should be withdrawn.

Discussion of Written Description Rejection

The Office Action rejects claims 1, 6-10, 13-19, and 21 under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description. The rejection is traversed for the reasons set forth below.

The Office Action contends that the specification does not disclose a representative number of species of the genera "heterologous sorting signal" and "heterologous signal peptide." According to the Office Action, the only species of heterologous sorting signal and heterologous signal peptide disclosed in the application are the LAMP-1 sorting signal and the LAMP-1 signal sequence.

An inventor is not required to describe every detail of his invention. Indeed, Applicants' disclosure obligation varies according to the art to which the invention pertains. M.P.E.P. § 2163. The structures and sequences of numerous sorting signals and signal peptides were well known in the art well before the present application was filed. For example, Thomas et al., *J Cell Sci.*, *116*(Pt 11): 2213-22 (2003) (enclosed herewith), discloses the sequence of the sorting signal of the connexin43 protein which directs it to lysosomes. Klionsky et al., *J Biol Chem.*, *265*(10): 5349-52 1990 (enclosed herewith), discloses the sequence of sorting signals for the vacuolar membrane protein repressible alkaline phosphatase. Hogue et al., *Biochem. J.*, *365*(Pt 3): 721-730 (2002) (enclosed herewith), discloses the sequence of the sorting signal of lysosome-associated protein transmembrane 4 alpha (LAPTM4 alpha). Sequences of numerous signal peptides are disclosed in, for example, Alberts et al. (eds.), *Molecular Biology of the Cell,* 3rd Edition, Garland Publishing Inc, New York (1994), Lehninger et al. (eds.), *Principles of Biochemistry*, 2nd Edition, Worth Publishers, New York (1993), and Nothwehr et al., *Bioessays, 12*: 479-484 (1990).

Thus, in view of the disclosure of the specification and the knowledge in the art at the time the subject application was filed, one of ordinary skill in the art would have understood that Applicants had possession of the claimed invention, which is defined using the terms "heterologous sorting signal" and "heterologous signal peptide." As such, the written description rejection under Section 112, first paragraph, is improper and should be withdrawn.

Discussion of Enablement Rejection

The Office Action rejects claims 1, 6-10, 13-19, and 21 under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement. According to the Office Action, the present specification enables a serotype 5 adenoviral vector comprising a nucleic acid sequence comprising SEQ ID NO: 1 and a cleavable LAMP-1 sorting signal operably linked to a CMV IE promoter-enhancer. The present specification, however, allegedly does not enable a gene transfer vector comprising a nucleic acid sequence comprising SEQ ID NO: 1 and any heterologous sorting signal or signal peptide that lacks a promoter sequence, transduction of antigen presenting cells by the gene transfer vector, and a pharmaceutical composition comprising the gene transfer vector. The rejection is traversed for the reasons set forth below.

With respect to enablement of the heterologous sorting signal and heterologous signal peptide, the Office Action alleges that, because the only operable heterologous sorting signal disclosed in the application is the LAMP-1 sorting signal, the specification only enables the use of the LAMP-1 sequence. The enablement standard does not require that Applicants disclose every operable embodiment of a particular invention. Instead, the test of enablement requires that an application contain sufficient information regarding the subject matter of the claims so as to enable one skilled in the art to make and use the claimed invention without undue experimentation. M.P.E.P. § 2164.01. Moreover, a specification need not disclose, and preferably omits, what is well-known to those skilled in the art. *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q. 2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984). See also M.P.E.P. § 2164.05(a).

As discussed above with respect to the written description rejection, the structures and sequences of numerous sorting signals and signal peptides, particularly sorting signals that direct proteins to lysosomes, were well known in the art well before the present application was filed. Thus, using only routine molecular biology techniques, one of ordinary skill in the art would have been able to make and use the claimed invention using any suitable sorting

signal in view of the disclosure of the present specification coupled with the knowledge in the art at the time the application was filed.

According to the Office Action, because claim 1 does not require operable linkage to a promoter, one of ordinary skill in the art would not know how to use a nucleic acid sequence comprising SEQ ID NO: 1 without conducting undue experimentation. Applicants respectfully disagree. Again, a claim need not recite every operable embodiment in order to satisfy the enablement requirement. The fact that claim 1 does not recite that the nucleic acid sequence is operably linked to a promoter does not preclude enablement of claim 1. The level of skill in the art is such that an ordinarily skilled artisan would understand that, in order to express a particular gene in a cell, the gene must be linked to a promoter. In addition, the specification discloses numerous examples of promoters suitable for use in the invention (see, e.g., paragraph [0037]). Thus, one of ordinary skill in the art would have been more than adequately equipped to make and use the claimed adenoviral vector given the high level of skill in the art, and the disclosure of the subject application.

The Office Action further alleges that the subject matter of claim 19 is not enabled by the present specification. Specifically, the Office Action contends that the specification does not teach any means for targeting the claimed gene transfer vector to antigen presenting cells *in vivo*. Applicants respectfully disagree. The specification discloses that adenovirus infection of dendritic cells (DC) is mediated by the interaction of the RGD domain of the penton base protein and integrin molecules expressed at the DC (cell surface (see paragraph [0048]). In addition, the specification discloses that dendritic cells can be targeted by the adenoviral vector by modifying the fiber protein to contain an RGD domain (see paragraph [0048]). The specification also discloses that an adenovirus containing deletions of the fiber CAR domain and penton RGD domain recognize and infect antigen presenting cells in the liver more efficiently than an adenovirus comprising wild-type coat proteins (see paragraph [0049]). Thus, the present specification enables the subject matter of claim 19.

The Office Action alleges that claim 21 is not enabled by the present specification because the specification does not demonstrate that the claimed gene transfer vector produces a protective immune response *in vivo*.

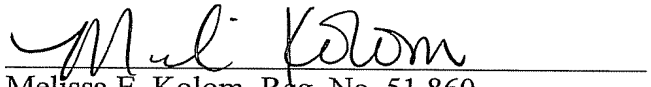
Whether or not the claimed gene transfer vector produces a protective immune response *in vivo* is of no consequence to the enablement of a pharmaceutical composition comprising the adenoviral vector and a pharmaceutically acceptable carrier. In any event, claim 21 has been amended to delete the term "pharmaceutical." Applicants note that the specification discloses how to prepare a composition comprising the claimed gene transfer vector and a pharmaceutically acceptable carrier (see, e.g., specification at paragraphs [0054] to [0063]). In addition, the specification discloses methods for administering the composition to a mammal to induce an immune response (see, e.g., Examples 2-4).

Therefore, in view of the foregoing, the amended claims are enabled by the present specification. As such, Applicants request withdrawal of the enablement rejection under Section 112, first paragraph.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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